Tetrahedron Letters No.26, pp. 2493-2495, 1967. Pergamon Press Ltd. Printed in Great Britain.

PHOTOCHEMICAL FORMATION OF BERBERINE ALKALOIDS FROM PROTOPINE ALKALOIDS

X. A. Dominguez and Jesus Garcia Delgado
Department of Chemistry, Instituto Tecnologico y de
Superiores de Monterrey, Monterrey, Mexico

W. P. Reeves
Department of Chemistry, Texas Lutheran College, Seguin, Texas

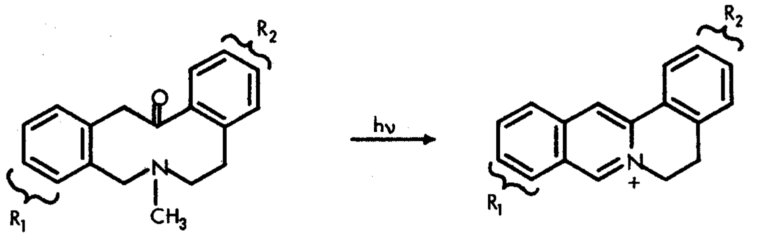
P. D. Gardner
Department of Chemistry, University of Utah, Salt Lake City, Utah

(Received 17 April 1967)

a-Allocryptopine (I), cryptopine (II) and protopine (III) comprise a family of alkaloids which is interesting spectroscopically in that each member possesses transannular carbonyl and tertiary amine functions in a ten-membered ring. A significant ground state interaction between these two functions has been shown to exist (1). We report here a new type of photochemical transformation of these three substances to corresponding members of the berberine family, berberine (IV), epiberberine (V) and coptisine (VI).

Irradiation of a dilute solution of cryptopine (II) in 95% ethanol under pure nitrogen for 100 hours afforded, after chromatography on silica gel and recrystallization from 95% ethanol saturated with picric acid, epiberberinium picrate (34%), m.p. 220-223° (dec) (3). The reaction was monitored by observing the disappearance of the ultraviolet maximum at 286 mμ and appearance of bands at 350 and 460 mμ. A similar experiment with protopine (III) gave a 23% yield of coptisine (VI), m.p. and mixed m.p. 215-217° (4). The product and authentic coptisine gave identical ultraviolet and infrared spectra and ran together on three dimensional TLC.

Irradiation of α-allocryptopine (I) afforded berberine (VI) which was isolated as berberinium nitrate, m.p. 255-258°. It was identical in all respects with an authentic sample.



I (R_1 = CH_3O, CH_3O
R_2 = CH_2O_2)

II (R_1 = CH_2O_2
R_2 = CH_3O, CH_3O)

III (R_1 = R_2 = CH_2O_2)

IV (R_1 and R_2 as in I)

V (R_1 and R_2 as in II)

VI (R_1 and R_2 as in III)

It is interesting to note that the use of chloroform in place of ethanol or methanol as the irradiation solvent gave the same products but at a more rapid rate and in higher yield. Thus, α-allocryptopine gave a 76% yield of berberine (as the nitrate) by simple recrystallization of the photomixture. It seems quite possible that a different mechanism is operative in halogenated solvents which are known to be good radical sources under conditions of ultraviolet irradiation. The reaction is undoubtedly very complex in alcohol solvents. The irradiation of protopine, for example, when monitored by TLC showed the presence of five transient species in addition to starting material and product. At the termination of the run, only the yellow spot (UV) due to coptisine remained. It is obvious that the identification and sequential appearance of these intermediates must be established before a mechanism can be deliniated.

Acknowledgement. This work was supported in part by National Institutes of Health Grant GM 07861.

REFERENCES

1. E. H. Mottus, H. Schwarz and L. Marion, Can. J. Chem., 31, 1147 (1953). The generality of this interaction in the ground state and in some cases in the excited state as well has been described by Leonard and co-workers (2).
2. N. J. Leonard, Record Chem. Progr., 17, 243 (1956). N. J. Leonard, J. A. Adamcik, C. Djerassi and O. Halpern, J. Am. Chem. Soc., 80, 4858 (1958). N. J. Leonard, T. W. Milligan and T. L. Brown, ibid., 82, 4075 (1960).
3. W. H. Perkin, Jr., J. Chem. Soc., 113, 492 (1918) reports m.p. 222° (dec).
4. We are indebted to Professor J. Slavic, Department of Medicinal Chemistry, Purkyne University, Czechoslovakia for an authentic sample of coptisine.